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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/788,426	03/01/2004	Jacques Dumas	BAYER-0044	4965
23599 7590 11/19/2010 MILLEN, WHITE, ZELANO & BRANIGAN, P.C. 2200 CLARENDON BLVD. SUITE 1400 ARLINGTON, VA 22201				
EXAMINER REESE, HEIDL				
ART UNIT		PAPER NUMBER		
1625				
NOTIFICATION DATE		DELIVERY MODE		
11/19/2010		ELECTRONIC		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

docketing@mwzb.com

### Office Action Summary

**Application No.**

10/788,426

**Applicant(s)**

DUMAS ET AL.

**Examiner**

Heidi Reese

**Art Unit**

1625

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-13, 24-30 and 32-43 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-13, 24-30, and 32-43 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/GS/US)  
Paper No(s)/Mail Date \_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_

### DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(c), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(c) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 29, 2010, has been entered.
2. Claims 1-13, 24-30, and 32-43 are pending in this application.

### *Claim Objections*

3. Claim 3 is objected to because the word "or" is missing from the last combination. Claim 4 is objected to because of the presence of repeating commas in line 3 on page 5 and line 2 on page 6. Appropriate correction is required.

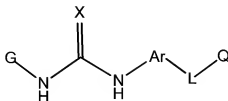
### *Claim Rejections - 35 USC § 103*

4. The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

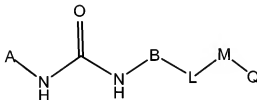
5. Claims 1-13, 24-30, and 32-43 are rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,492,393 to Breitfelder *et al.* and U.S. Patent No. 7,202,244 to Boyle *et al.*, in view of Silverman.
6. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:
  1. Determining the scope and contents of the prior art.
  2. Ascertaining the differences between the prior art and the claims at issue.
  3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.
7. Breitfelder '393 teaches compounds of formula I below



where G is a saturated or unsaturated mono or bicyclic carbocycle or heterocycle; X is O or S; Ar is phenyl, naphthyl, quinolyl, tetrahydroquinolyl, and several others; L is a carbon chain, which may include O, N, and/or S, and which may include oxo-substitution on carbons in the chain; and Q is an optionally substituted phenyl, naphthyl, pyridyl, and numerous other cyclic moieties. Possible substituents for Q include C<sub>1-6</sub> alkoxy. Breitfelder teaches that such compounds have activity as inhibitors of cytokine production (i.e., in a cell signaling pathway) and are potentially useful in treating many diseases.

8. Claim 1 is directed to a compound of the formula shown below



where A is a bicyclic heterocycle; B is phenyl, naphthyl, or pyridyl; L is (CH<sub>2</sub>)<sub>0-4</sub>-O<sub>0-1</sub>-(CH<sub>2</sub>)<sub>0-4</sub>; (CH<sub>2</sub>)<sub>0-4</sub>-(CO)<sub>0-1</sub>-(CH<sub>2</sub>)<sub>0-4</sub>; (CH<sub>2</sub>)<sub>0-4</sub>-(NR<sup>3</sup>CO)<sub>0-1</sub>-(CH<sub>2</sub>)<sub>0-4</sub>; (CH<sub>2</sub>)<sub>0-4</sub>-(CONR<sup>3</sup>)<sub>0-1</sub>-(CH<sub>2</sub>)<sub>0-4</sub>; (CH<sub>2</sub>)<sub>0-4</sub>-S<sub>0-1</sub>-(CH<sub>2</sub>)<sub>0-4</sub>; (CH<sub>2</sub>)<sub>0-4</sub> NR<sup>3</sup><sub>0-1</sub>-(CH<sub>2</sub>)<sub>0-4</sub>; or a single bond; M is pyridine, and Q is a substituent which may be an ester, ether, aldehyde, carboxylic acid, or amide group. Note that M corresponds to Q in Breitfelder '393. Dependent claims 22-12 narrow the possibilities for ring A and linking group L. Claim 13 is directed to pharmaceutical compositions. Claims 24-30 encompass the subgenus where B is phenyl. Claim 32-43 encompass the subgenus where B is

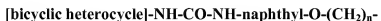
quinolyl. The asserted utility is activity in cancer therapy, based on activity in the ras signal pathway.

9. But for the options, in the present case, i) that B may be pyridine and ii) that terminal ring M (corresponding to Q is Breitfelder '393) may bear an ester, aldehyde, carboxylic acid, or amide group, the genus of claim 1 would fit entirely within the genus taught by Breitfelder.

10. Specific compounds taught by Breitfelder include i) about 40 compounds with the core G-NH-CO-NH-naphthyl-linker-pyridine (*e.g.*, col 45, cpds 1 and 2, col. 47, cpd 1, col. 53, cpd 1, col 55, cpds 1.4, col. 59, cpds 1,2,3,4, col 61, cps 1,2,3,4, col. 63, cpds 2,3,6, col 67, cpd 1, col 69, cpd 5, col 63, cpds 2,3,6, col 71, cpds,5, col 73 cpds 2,3,4), ii) many compounds with



(cols 37, 39, 41, and 51), including one with Q = pyridine (col 53, 1<sup>st</sup> compound); and iii) several compounds with B = tetrahydroquinolyl and Q = pyridine (col 67, cpd,5, col 69 cpds 1,2, col 71 cpd 5, col 73 cpd 5, ); a great many with the structural element



such as the first compound shown in col 53; several compounds of the type



(col 39, compounds 3 and 5, col 41, compound 1), and many compounds of the type



(col 67, all 5 compounds, col 69, all 6 compounds, col 71, all 6 compounds; col 73 all 5 compounds; col 75 all 6 compounds).

11. In summary, among the compounds taught by Breitfelder '393, a large number have at least four of the five core subunits claimed in generic claims of the present application: A = bicyclic heteroaryl; NHCONH; B = phenyl, naphthyl, (tetrahydro)quinolyl; L = carbon chain and/or -O- and/or CO or NHCO; M = pyridine.

12. Moreover, Boyle '244 teaches phenyl pyridyl ureas, phenyl pyrimidyl ureas, and phenyl diazinyl ureas, as well as quinolyl ureas as chk-1 inhibitors, for example at col. 9 lines 60-65, col 17, lines 50-65, col 18, lines 5-15, and col 18, lines 45-54 (quinolyl).
13. Silverman p. 32 teaches that phenyl and pyridyl are isosteres. Moreover, if phenyl and pyridyl are isosteres, then their benzo-fused analogues, naphthyl and quinolyl are also isosteres.
14. Given the very common technique in the art of drug discovery of structure variation, the known isosteric properties of phenyl/pyridyl and naphthyl/quinolyl/isoquinolyl (see Silverman excerpt), and the objective of maximizing activity against enzymes in cellular signaling pathways, it would be obvious to merely vary the combinations of the structural elements taught by Breitfelder '393 and also to augment these elements with the pyridyl-urea element taught by Boyle '244 to produce the claimed invention.

### *Conclusion*

**15. No claim is allowed.**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Heidi Reese, whose telephone number is (571) 270-5277. The examiner can normally be reached on Monday-Friday 8 AM - 5 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, can be reached on (571) 272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Janet L. Andres/  
Supervisory Patent Examiner, Art Unit 1625

/H. R./  
Examiner, Art Unit 1625